UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

PC Code: 288201
Chemical: Pyrimethanil
DP Barcode: D387590
DECISION: 402624

July 26, 2011

MEMORANDUM

SUBJECT: Section 3 New Use: Ecological Risk Assessment for the proposed use of pyrimethanil (co-formulated with fluopyram) on almond, apple, pistachio, potato, stone fruit (except cherries), and wine grapes.

TO: Shaja Joyner, Risk Manager, RM 20
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THROUGH: Dana Spatz, Branch ~~Chief~~ 7/26/11
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Bayer Corporation is seeking to add new uses for an end-use product containing pyrimethanil (PC Code 288201) and fluopyram (PC Code 080302) as the active ingredients[1]. This product is a co-formulation of pyrimethanil with fluopyram, which are fungicides belonging to different

[1] "Fluopyram/Pyrimethanil 500 SC": 11.3% Fluopyram and 33.8% Pyrimethanil (EPA Reg. No. 264-RNIL, 01/24/11).

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chemical groups and having different modes of pesticide action. Pyrimethanil's (anilino-pyrimidine) mode of action is inhibition of or interference with methionine biosynthesis and secretion of hydrolytic enzymes necessary for infection in several plant pathogenic fungi species. Fluopyram's (pyridinyl-ethyl-benzamide) mode of action is inhibition of mitochondrial respiration through inhibiting electron transport. The focus of the present ecological risk assessment is on pyrimethanil alone. The proposed crop uses, almond, pistachio, apple, potato, stone fruit (except cherry), and wine grapes, are currently registered for pyrimethanil use as the sole active ingredient (a.i.). An ecological risk assessment for pyrimethanil, an anilino-pyrimidine fungicide, was previously prepared for the use of fluopyram/pyrimethanil mixture[2] on small berries (bush and caneberries; D360931, 05/18/10). The patterns for currently registered uses of pyrimethanil as the sole active ingredient[3] include those currently proposed for the co-formulation[1] (*i.e.*, but not the small berries) plus bulb vegetables (onion, garlic, leek, shallot), pome fruits (pear, crabapple, loquat, mayhaw, quince in addition to apple), strawberries, tomatoes, tree nuts[4], and tuberous and corm vegetables (others in addition to potato); all of these uses were considered in a previous risk assessment (D283997, 03/31/04).

Proposed Use

This petition is for pyrimethanil only when it is co-formulated with fluopyram (EPA Reg. No 264-RNIL, dated 01/24/11). The proposed crop uses are almonds, pistachio, apple, potato, stone fruit (except cherry), and wine grapes which constitute uses that are currently registered for pyrimethanil. The bulb vegetables, other pome fruits, other tuberous and corm vegetables, strawberry, tomato, and other tree nut uses are not included under this petition. All of these uses were previously assessed when pyrimethanil was the sole active ingredient (a.i.) (D283997, 03/31/04).

The proposed maximum single application rate for pyrimethanil (either as sole a.i. or as the co-formulated a.i) is 0.70 lb a.i./acre with a seasonal maximum annual application rate of 1.3 lbs a.i./acre (for the co-formulated a.i.) and 2.14 lbs. a.i./acre (for the sole a.i. product) and a minimum reapplication interval of 7 days **(Table 1)**. This assessment assumes that the maximum seasonal rate equals the maximum yearly rate (*i.e.*, 1.3 lbs a.i./acre/year). The proposed maximum application rates and total maximum application rates per year are either equivalent or below the rates previously assessed.

[2] "Fluopyram/Pyrimethanil 500 SC" 11.9% Fluopyram and 33.8% Pyrimethanil
[3] SCALA™ SC Pyrimethanil Fungicide (34.7% a.i.)
[4] Current labels 264-708, 264-788, and 264-1028 limit use to only almonds and pistachios.

Table 1. Use patterns and maximum single and seasonal application rates for currently registered pyrimethanil[a] uses and to those under the proposed co-formulation[b] label			
Use Pattern (*examples*)	**Single App. Rate** *lbs a.i./A*	**App. Rate per year[d]** *lbs a.i./A*	**App. Interval** *days*
Almond and pistachio[a]	0.7[c]	2.14	7
almond and pistachio[b]	0.66	1.3	7 - 14
Stone fruits[a,b], *except cherries* (apricot, nectarine, peach, plums, plumcot, prune)	0.7	2.14	7
	0.27	1.09	7 - 14
Bulb vegetables[a] (onion, garlic, leek, shallot)	0.7	2.1	7 - 14
Strawberries[a]	0.7	2.14	7 - 14
Pome fruits[a] (apple, pear, crabapple, loquat, mayhaw, quince)	0.39	1.62	7
apple[b]	0.39	1.3	7 -10
Grapes[a]	0.7	1.43	7
wine grapes[b]	0.66	1.3	12 - 21
Tuberous and corm vegetables[a] (potato, sweet potato, arracacha, arrowroot, artichoke, edible canna, cassava, chayote, chufa, dasheen, ginger, leren, tanier, tumeric, yam bean, true yam)	0.26	1.36	7 - 14
potato[b]	0.27	0.82 (aerial); 1.06 (other)	7 - 14
Tomato[a]	0.27	1.4	7 - 14

[a] The maximum registered under end-use products containing pyrimethanil ; non-shaded cells:
[1] 207-705 SCALA™ 400 SC Pyrimethanil Fungicide (37.4 % a.i.; 3.34 lb a.i./gallon)
[2] 264-788 SCALA™ SC Pyrimethanil Fungicide (54.6 % a.i.; 5.0 lb a.i./gallon)
[3] 264-1024 DISTINGUISH™ 480 SC Fungicide (38.8 % a.i., 3.51 lb a.i./gallon)

[b] The uses are listed under the end-use product Fluopyram/Pyrimethanil 500 SC (33.8 % pyrimethanil a.i.); shaded cells considered in this assessment.

[c] No more than two consecutive applications may be made without alternating to a fungicide with a different mode of action.

[d] Maximum application rate per season is assumed to be equivalent to maximum application rate per year.

Label Amendments

The use rates for strawberries are not specified on the label; strawberry uses were not considered in this assessment. Therefore, label text referencing use of the co-formulated product on strawberries should be omitted from the label.

Risk Conclusions

The risk conclusions for pyrimethanil from the proposed uses of pyrimethanil/fluopyram are nearly the same as previously assessed, because the proposed use rates are consistent with the maximum rates previously considered for pyrimethanil alone (D283997, 2004). For a detailed summary of ecotoxicology data and risk quotient (RQ) calculations refer to the new use assessment (D283997, USEPA 2004). The risk conclusions relevant to the currently proposed use sites were either extracted from the cited assessment (for Pyrimethanil Technical Fungicide, 98.5% a.i. EPA Reg No. 264-TNU; and SCALA SC Pyrimethanil Fungicide, 37.4% a.i., EPA Reg. No. 264-TNL) or determined again with application rates in Table 1 for tree nuts (which only include almonds and pistachios), stone fruits (except cherries), bulb vegetables, strawberries, pome fruits (which includes apples), grapes, tuberous and corm vegetables (which includes potatoes), and tomatoes and are presented below.

Based on a screening level risk assessment and projection of use (to stone fruit *(except cherries)*, wine grapes, tree nuts *(almonds, pistachios)*, pome fruit *(apple)*, tuberous and corm vegetables *(potato)*) at the maximum application rate, pyrimethanil is predicted to pose chronic risk to both non-listed and listed birds and mammals. Pyrimethanil is not expected to pose an acute risk to terrestrial animals or aquatic plants and animals. The use of pyrimethanil is not expected to pose a risk to honeybees.

Chronic risk to aquatic animals is also not expected except in the cases of estuarine/marine fish. Estuarine/marine fish are more acutely sensitive (sheepshead minnow, 96 hr LC_{50} = 2.8 mg/L *moderately toxic*, MRID 45657005) to pyrimethanil than freshwater fish (rainbow trout, bluegill sunfish, mirror carp; 96 hr LC_{50} = 10.1, 26.2, 36.5 mg/L, respectively, *slightly toxic*; MRIDs 456570-08, -09, -10). An early life-stage freshwater fish study (MRID 456570-13) on the rainbow trout yielded a NOAEC of 0.02 mg/L. A supplemental estuarine/marine full life-cycle toxicity test (MRID 475169-01) with sheepshead minnow (*Cyprinodon variegatus*) indicated a NOAEC < .019 mg/L; meanwhile the acute-to-chronic ratio calculation yields a NOAEC of 0.0055 mg/L (= [2.8 *0.02]/10.1). Taking the calculated NOAEC into consideration for RQ calculation, yields an exceedance of the chronic LOC (=1) for listed and non-listed estuarine/marine fish (RQ = 2.34 for aerial uses on tree nuts; for EECs see Table 6 of USEPA 2004). Given the indeterminate nature of the estuarine/marine chronic endpoint, <u>chronic risk to estuarine/marine fish is assumed</u>.

The potential for risk to listed and non-listed terrestrial plants is unknown; however, given evidence of phytotoxicity in cherries (see 'Data Gaps' section below), risk to terrestrial plants is assumed. The potential for risk to terrestrial plants and animals from pyrimethanil degradates is unknown and is uncertain for aquatic life. The pyrimethanil degradate 2-amino-4,6-dimethylpyrimidine is considered to be a degradate of toxicological concern for the human drinking water assessment; it is expected to be more resistant to aerobic degradation and more mobile than the parent compound. No toxicity data on terrestrial animal or plant life with the degradate have been submitted, but by extrapolation from human health concerns and the fact that it could be formed in the environment, it is also considered to be of potential ecotoxicological concern for terrestrial animals. Two acute studies on the degradate of concern (AE F132593), 4,6-dimethylpyrimidine-2-amine, using freshwater fish (MRID 46268601) and waterflea (MRID 46268602) were reviewed at the time of the last assessment (USEPA 2010; DP Barcode 360931). Sublethal effects (surfacing and lethargy) were observed at the highest concentration tested in the trout study; however, the study is classified supplemental (qualitative use only) because water solubility was not reported, a dark fine sediment was observed at the three highest concentrations, and there was no mention of centrifugation in the study; the endpoint was non-definitive (LC_{50}>97.43 mg total a.i./L). No effects were observed at any level in the waterflea study (EC_{50}>98.28 mg/L). Combined residues of pyrimethanil and the major degradate (total toxic residues) were used in calculating aquatic ecological effects concentrations. For detailed summaries of the available ecological toxicity data see Appendix A of D283997, US EPA 2004 and Table 5,6, and 7 of D360931, US EPA 2010.

Aquatic Animals
Aquatic risk quotients for the proposed uses of pyrimethanil are <0.05 (acute) and <1 (chronic) where data is available, which are below the acute listed species LOC and the chronic LOC for aquatic animals, respectively. Acute risk to freshwater fish/invertebrates and estuarine/marine fish/invertebrates is <u>not expected</u> as a result of pyrimethanil use on stone fruit *(except cherries)*, wine grapes, tree nuts *(almonds, pistachios)*, pome fruit *(apple)*, tuberous and corm vegetables *(potato)*) at the proposed maximum application rates. However, <u>chronic risk to estuarine/marine fish is assumed</u> and chronic risk to freshwater fish/invertebrates as well as estuarine/marine invertebrates is <u>not expected</u>.

Aquatic plants
No LOC is exceeded for vascular or non-vascular aquatic plants potentially exposed from maximum applications of pyrimethanil. Risk to aquatic plants is <u>not expected</u> as a result of pyrimethanil use on stone fruit *(except cherries)*, wine grapes, tree nuts *(almonds, pistachios)*, pome fruit *(apple)*, tuberous and corm vegetables *(potato)*) at the proposed maximum application rates.

Terrestrial animals
<u>Birds and Mammals</u> –acute
Since pyrimethanil is classified as practically non-toxic to birds (northern bobwhite, LD_{50} >2012 mg/kg-bw, MRID 45657015; northern bobwhite, mallard duck, LC_{50}s >4874, >5132 mg/kg, respectively, MRIDs 456570-18, -19) and mammals (toxicity category III; rat, ♂LD_{50}: 4149 mg/kg in males, 5971 mg/kg in females, MRID 43345002), acute risks to birds and mammals are presumed to be negligible from any of the proposed uses. No mortality or signs of intoxication were reported at any test concentration for the acute bird studies with the exception of body weight gain reductions in some treatment groups of the dietary studies; clinical observations in the acute rat study included reduced activity, reduced muscle tone, prostration, body soiling, urogenital soiling, ataxia, and hunched posture. Furthermore, if the highest doses tested in the avian studies are considered the endpoint, acute RQs for birds exceed Agency LOCs (for

restricted use and listed species) for the smallest size class (20g bird; RQs 0.13-0.23; application rate for tree nuts and grapes of 0.66 lbs a.i./A applied 2x with a 7 day interval; 35 day half life; TREX v. 1.4.1); however, given that the calculation is based on the dose study for which there was no mortality or sublethal effects, which yielded a non-definitive endpoint, the actual RQs are expected to be below the calculated values. Acute avian dietary-based RQs (also based on non-definitive acute dietary study endpoints) and mammalian dose-based RQs do not lead to Agency LOC exceedances. Therefore, acute risk to birds and mammals is not expected as a result of pyrimethanil use on stone fruit *(except cherries)*, wine grapes, tree nuts *(almonds, pistachios)*, pome fruit *(apple)*, tuberous and corm vegetables *(potato)*) at the proposed maximum application rates.

Birds – chronic

For multiple applications (application rate for tree nuts and grapes of 0.66 lbs a.i./A applied 2x with a 7 day interval; 35 day half life; TREX v. 1.4.1) of pyrimethanil, the chronic (and listed species) LOC is exceeded for birds on a dietary-basis and feeding on short grass (RQ = 1.95) and broadleaf plants/small insects (RQ= 1.1) at tree nut and grape use sites. The avian reproduction study (mallard duck, MRID 45657022) yielded a NOAEC of 152 mg/kg-diet based on adverse effects on the number of eggs laid, eggs set, the number of viable and live embryos, and the number of 14-day survivors. The chronic LOC is exceeded for all other proposed uses as well which have slightly lower application rates (see Table 1). Chronic risk to birds is expected as a result of pyrimethanil use on tree nuts (almond, pistachio), wine grapes, apples, potato, and stone fruits *(except cherries)* at the proposed maximum application rates.

Mammals – chronic

For multiple applications (application rate for tree nuts and grapes of 0.66 lbs a.i./A applied 2x with a 7 day interval; 35 day half life; TREX v. 1.4.1) of pyrimethanil, the chronic (and listed species) LOC is exceeded for mammals on a dose-basis and feeding on short grass (RQ = 2.94-6.43), tall grass (RQ= 1.35-2.95), and broadleaf plants/small insects (RQ= 1.66-3.62) at tree nut and grape use sites. The 2-generation rat study (MRID 43301623) yielded a NOAEL of 400 mg/kg-diet (adjusted dose-basis is 20 mg/kg-bw) based on decreased mean body weights and body weight gains as well as decreased pup body weights on lactation at day 21 of the study. The chronic LOC is exceeded for all other proposed uses as well which have slightly lower application rates (see Table 1). Chronic risk to mammals is expected as a result of pyrimethanil use on tree nuts (almond, pistachio), wine grapes, apples, potato, and stone fruits *(except cherries)* at the proposed maximum application rates.

Terrestrial invertebrates

A honey bee (*Apis mellifera*) acute contact and oral study using the TGAI (95.9% a.i.) indicates that pyrimethanil is practically non-toxic to bees (>100 µg/bee, MRID 45657023). Acute risk to bees is, therefore, not expected as a result of pyrimethanil use and no honey bee label language is required on the label.

Uncertainties

Given the lack of data utilizing co-formulated product, the effect of fluopyram (synergistic, antagonistic, or none) on the toxicity of pyrimethanil to wildlife and plant life is unknown.

Comparisons of rat data on pyrimethanil alone with a mixture of pyrimethanil and fluopyram are inconclusive. The initial acute rat oral study on the technical (98.4% a,i.; MRID 43345002) was a definitive study (5 groups of 10 rats 50:50 male:female with the following concentrations: 0, 800, 1600, 3200, and 6400 mg/kg); there were 8 deaths at the highest concentration tested and the survivors gained weight. The acute oral LD_{50}s were definitive: 4149 mg/kg in males, 5971 mg/kg in females. However, the more recent acute oral study on the co-formulation (Fluopyram – 11.2% w/w; Pyrimethanil - 33.8% w/w; MRID 47567311) was a limit test (2 groups of 3 females at 2000 mg/kg bw without a control group); there were no mortalities and all animals gained weight. The acute oral LD_{50} was not definitive: >2000 mg/kg-bw. Both studies, however, indicated sublethal effects such as reduced activity/motility. Chronic studies (2-generation reproduction) suggest greater sensitivity to fluopyram (NOAEL: ♂ 15 mg/kg-bw; ♀18 mg/kg-bw; MRID 47372447) than to pyrimethanil (NOAEL: ♂ 23.1 mg/kg-bw; ♀27.4 mg/kg-bw; MRID 43301623) (Appendix I).

In addition, it is unclear whether potential synergistic effects with fluopyram may result in altering the risk conclusion for freshwater invertebrates (*i.e.*, waterflea, *Daphnia magna*). An increase in sensitivity by an order of magnitude (as witnessed in the mixture of fluopyram: trifloxystrobin with a percent purity adjustment for trifloxystrobin and a comparison of green algae studies, USEPA 2011) would change the risk picture for strawberries and bulb vegetables (uses not in this proposal; RQs[5] of 0.13-0.23 with acute freshwater invertebrate assumed endpoint value of 0.3 mg a.i./L) as well as applications to tree nuts (one of the uses proposed at this time; RQs[5] approximately ranging from 0.05 to 0.14 with endpoint values of 0.3 to 0.1 mg a.i./L assumed for freshwater invertebrates; *i.e.*, an exceedance of the acute listed species LOC of 0.05 and acute restricted use LOC of 0.1). Additional uncertainty in these estimates is characterized by differential runoff potential of fluopyram and pyrimethanil in co-formulation, which may lead to reduced EEC values from those used to calculate the latter RQs. Furthermore, comparison of additional available pyrimethanil single a.i. and fluopyram single a.i. data (Appendix I) suggest that freshwater invertebrates and green algae are more sensitive to pyrimethanil than to fluopyram. An additive effect of fluopyram to the toxicity of pyrimethanil is assumed as a potentiality, but is not conclusive. Additional data on freshwater invertebrates (and green algae, but potentially other taxa as well) using co-formulated products (pyrimethanil and fluopyram) may clarify if the toxicities of the two active ingredients in this new formulation have an additive effect.

Data Gaps

Data gaps included in this assessment are identical to those presented in previous assessments and are summarized below with updates and additional data requests since the last assessment (D360931, 05/18/10):

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[5] The RQ values are based on PRZM/EXAMS EECs calculated using total residues of single a.i. pyrimethanil and its major degradate 2-amino-4,6-dimethylpyrimidine including estimated concentrations generated from spray drift and runoff; the EECs would be appreciably reduced when the contribution via runoff is subtracted from the EEC estimates as is the case when co-formulated products are considered.

Fate:

Analytical Chemistry Methods: The registrant has not addressed the guideline data requirement OPPTS 850.6100 for the Environmental chemistry methods and associated independent laboratory validation.

This deficiency was previously noted (D283997) that the registrant did not submit any analytical chemistry methods to identify and quantify residues of pyrimethanil and its degradates in water or soil/sediment, as required by the Pesticide Assessment Guidelines (OPP 00405, May 3, 1995). Therefore, the registrant must submit independently validated analytical chemistry methods to identify and quantify residues in water and soil/sediment. The methods must be sufficiently sensitive to adequately determine NOAEC, EC_{05}, and characterize residues in water and soil/sediment resources. The value of this information is high as it needed to identify and quantify pyrimethanil residues in the environment at concentrations of ecological importance, to verify and monitor concentrations of parent and degradates in the above recommended aquatic tests, and to provide a means to assess irrigation water impacts, should that become necessary.

Effects:

Fish Full Life-Cycle Testing: A Freshwater Fish Life Cycle test (OPPTS GLN 850.1500) was requested by EFED at the time of the last assessments (D283997, USEPA 2004; D360931, USEPA 2010) and again in a review of waiver request memorandum (D317462, USEPA 2005[a]). The EFED concurred (D317462, USEPA 2005[b]) with the following registrant proposals: 1) to do a fish full life cycle study on *estuarine species* because estuarine fish are more sensitive than freshwater fish[6]; 2) to cancel the requirement for an Estuarine/Marine Fish Early Life Stage study (OPPTS GLN 850.1400), which was requested at the time of the second to last assessment, because the estuarine fish full life-cycle study would suffice. However, EFED also requested that the freshwater fish life-cycle study be reserved in case the estuarine life cycle study shows chronic risk. At this time, the estuarine/marine full life-cycle toxicity test (MRID 475169-01) with sheepshead minnow (*Cyprinodon variegatus*) is classified as supplemental without a definitive endpoint (NOAEC). The reason the study is supplemental is many-fold: 1) the age of the F_o generation at study initiation is unclear; 2) a NOAEC could not be determined from the study due to statistically-significant reductions ($p<0.05$) in F_o male wet weight at the lowest test level and biologically-relevant reductions (21-27%) suggestive of treatment-related effects at all test levels; 3) there were only two replicates per treatment level in this study design, which greatly reduces the statistical power or ability to detect significant effects; replicate response (within treatments) was quite variable for a number of endpoints, including number of eggs/female/day and several F_1 endpoints on Day 28 post-hatch; interpretation of significant findings would have been facilitated if the replicate number was higher in this study. A new estuarine/marine fish full-life cycle study which addresses the guideline deviations of the submitted study is recommended.

Data Gap

- Estuarine/Marine Fish Full-Life Cycle Study (Guideline 850.1500) with sheepshead minnow, *Cyprinodon variegatus*, TGAI

[6] Presumably, on an acute toxicity basis.

Terrestrial Plant Testing: Tier II Seedling Emergence and Vegetative Vigor tests (OPPTS GLNs 850.4225 and 850.4250) were requested by EFED at the time of the last assessments (D283997, USEPA 2004; D360931, USEPA 2010) because label language warned of potential phytotoxic effects. The registrant submitted a waiver request (MRID 464150-02) and EFED recommended (D317462, USEPA 2005[a]) these studies be reserved pending a fuller explanation by the registrant of the basis for any phytotoxic warning on pyrimethanil labels. A response to the EPA review of the waiver request was then submitted (MRID 466854-02) with an explanation for the label warning of potential phytotoxic effects. This document indicated that the only evidence of phytotoxicity was in one test at a very high rate where sweet cherries were affected. As a result, registration on sweet cherries was not pursued. No additional information was provided to indicate what the effects were and at what level they were tested to provide a sense of whether similar effects might be possible to other plants at levels expected in the environment. The concern is that it might not be just sweet cherries that would be adversely affected by pyrimethanil; other species may also be susceptible. However, EFED agreed at the time (D317462, USEPA 2005[b]) to continue with these studies as in reserve, but asked that a summary of the referenced study be provided indicating the rate(s) at which the effect occurred and a description of the effect(s). A brief summary was provided (MRID 468983-01) in 2006 concluding that dwarf (tart) cherry trees would not be adversely impacted by SCALA at maximum rates (100 gpa) under cool or hot conditions, while sweet cherries could be impacted at the highest rate tested (3 applications at 18 fl. oz/A; 800 g a.i./ha = 0.714 lbs a.i./A; a total of 2400 g a.i./ha = 2.14 lbs a.i./A) in cool or hot weather conditions because the trees showed phytotoxicity after the second application and leaf burning of 20% of leaf surface by the third application. Since the latest assessment, Tier I (not Tier II) seedling emergence and vegetative vigor tests using TEP (Pyrimethanil SC 600) were submitted, MRIDs 48293001 and 48282301, respectively, and are pending review. However, the study author conclusions indicate statistically significant effect (below 25% effect level) for a representative monocot and dicot species in the seedling emergence study (MRID 48293001) at a single pre-emergence soil application rate of 1.4 lbs a.i.A (using Pyrimethanil SC 600, 54.47% pyrimethanil a.i.). In order to calculate a NOAEC for these species a definitive study is required; as a result, a Tier II seedling emergence study for at least these two species is required.

Data Gap

- Seedling Emergence, Tier II Study (Guideline 850.4225) for at least lettuce, *Lactuca sativa* and corn, *Zea mays*, TEP (single a.i. pyrimethanil)

Co-formulated data

In addition, data on co-formulated products (pyrimethanil and fluopyram) on terrestrial plants are requested to be held in reserve pending review of the submitted Tier I studies and the pending submittal and review of the Tier II study requested in this assessment. Given that a co-formulation of fluopyram with another fungicide (*i.e.*, trifloxystrobin) increases the sensitivity of plants to the trifloxystrobin (esp. in vegetative vigor study for dicots, see USEPA 2011, D385876, D387594; endpoints adjusted for trifloxystrobin from the mixed formulation are lower relative to single trifloxystrobin a.i. formulations) suggests that fluopyram may potentially increase the potency of fungicides with which it is mixed. This was particularly the case for non-vascular aquatic plants (green algae, *Pseudokirchneriella subcapitata*) for which the co-formulation adjustment for trifloxystrobin indicated an increase in sensitivity by an order of magnitude from 37.1 μg a.i./L (single trifloxystrobin a.i.) to 8.0 μg a.i./L (co-formulation adjusted to trifloxystrobin). However, additional data were requested for the fluopyram/trifloxystrobin formulation to confirm these comparisons. Nevertheless, a similar effect is possible with a co-formulated product of fluopyram and pyrimethanil.

In reserve

- Seedling emergence, Tier I (Guideline 850.4100) or Tier II (Guideline 850.4225), TEP (Fluopyram/Pyrimethanil 500 SC"; 11.3% Fluopyram and 33.8% Pyrimethanil (EPA Reg. No. 264-RNIL, 01/24/11))
- Vegetative vigor, Tier I (Guideline 850.4150) or Tier II (Guideline 850.4250), TEP (Fluopyram/Pyrimethanil 500 SC"; 11.3% Fluopyram and 33.8% Pyrimethanil (EPA Reg. No. 264-RNIL, 01/24/11))

References

USEPA 2004. New Use Chemical Review. Pyrimethanil Section 3. First food uses on tree nuts, stone fruits (except cherries), bulb vegetables, strawberries, pome fruits, grapes, tuberous and corm vegetables, and tomatoes – (Pyrimethanil Technical Fungicide, 98.5% a.i., EPA Reg. No. 264-TNU; and SCALA SC Pyrimethanil Fungicide, 37.4% a.i., EPA Reg. No. 264-TNL). DP Barcodes: D283997, D292509. OPPTS/ EFED, Washington, DC. March 31, 2004.

USEPA 2010. New Uses on small berries (caneberries and bushberries) in the co-formulated end –use product fluopyram/pyrimethanil 500 SC. DP Barcode: D360931. OPPTS/EFED, Washington, DC. May 18, 2010.

USEPA 2011. Ecological Risk Assessment for Use of Fluopyram/Trifloxystrobin 500 SC on Almonds, Apples, Cherries, Cucurbit Vegetables, Peanuts, Pecans, Pistachios, Potatoes, Sugar Beets, Stone Fruits, Tree Nuts, and Wine Grapes. DP Barcode(s): D385876, D387594. OCSPP/EFED, Washington, DC. June 13.2011.

USEPA 2005[a]. Review of Waiver Requests for Pyrimethanil. DP Barcode D317462. OPPTS/EFED, Washington, DC. September 21, 2005.

USEPA 2005[b]. Review of Followup to Waiver Requests for Pyrimethanil. DP Barcode D317462. OPPTS/EFED, Washington, DC. December 14, 2005.

Appendix I. Available Ecological Toxicity Data for Comparison with Fluopyram

Group	Species	Pyrimethanil Toxicity	Fluopyram Toxicity
Freshwater Fish	Rainbow Trout *Oncorhynchus mykiss*	TGAI (99.5%) LC_{50}: 10.1 mg a.i./L MRID 45657008 (Supplemental[1])	TGAI (94.7%) LC_{50}>1.78 mg a.i./L NOAEC:1.78 mg a.i./L MRID 47372328 TEP (41.5%) LC_{50} >46.4 mg a.i./L NOAEC: 1.31 mg a.i./L MRID 47372333
Freshwater Invertebrates	Water flea *Daphnia magna*	TGAI (99..3%) EC_{50}: 3 mg a.i./L MRID 45657004 (Acceptable)	TGAI (94.7%) EC_{50}>17 mg a.i./L NOAEC: 17 mg a.i./L MRID 47372324 (Acceptable) TEP (41.5%) EC_{50}>38.2 mg a.i./L NOAEC: 11.6 mg a.i./L MRID 47372325 (Acceptable)
Honey Bee Acute Contact	Honey bee *(Apis mellifera)*	TGAI (95.9%) LD_{50} >100 µg a.i./bee (acute contact and oral toxicity) MRID 45657023 (Acceptable)	TGAI (95.5% a.i.) LD_{50} >100 µg test material/bee MRID 47372347 (Acceptable) TEP (41.6%a.i.) LD_{50} > 83.2 µg a.i./bee MRID 47372348 (Acceptable)
Algae Acute	Green algae *Pseudokirchneriella subcapitata*	TGAI (95.5%) EC_{50}: 1.8 mg a.i./L NOAEC<0.3 mg a.i./L MRID 45657102 (Acceptable)	TGAI (94.7%) EC_{50}: 4.3 mg a.i./L NOAEC: 1.46 mg a.i./L 96 hours (biomass) MRID 47372403 (Acceptable) TEP (41.5%) EC_{50}: 3.4 mg a.i./L NOAEC: 1.17 mg a.i./L 72 hours (cell density) MRID 47372407 (Acceptable)
Rat Acute Oral	Rat	TGAI (98.4%) ♂LD_{50}: 4149 mg/kg ♀LD_{50}: 5971 mg/kg MRID 43345002 (Acceptable) TEP (33.8% pyrimethanil; 11.2% fluopyram): ♀LD_{50} >2000 mg/kg-bw MRID 47567311 (Acceptable)	TGAI (94.7%) ♀LD_{50} >2000 mg/kg-bw MRID 47372430 (Acceptable)
Rat 2-generation reproduction study	Rat	TGAI (96.75%) NOAEL: 400 mg/kg-diet (♂: 23.1 mg/kg-bw; ♀27.4 mg/kg-bw) MRID 43301623 (Acceptable)	TGAI (94.7%) *Parental & Offspring* NOAEL: 220 mg/kg-diet (♂: 15 mg/kg-bw; ♀18 mg/kg-bw) *Reproductive* NOAEL: 1,200 mg/kg-diet (♂: 83 mg/kg-bw; ♀96 mg/kg-bw) MRID 47372447

[1]Test concentrations were not measured at every treatment level